Tafasitamab and Lenalidomide Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
Tafasitamab in combination with lenalidomide followed by tafasitamab monotherapy for the treatment of adult patients with relapsed or refractory diffuse large B cell lymphoma (DLBCL) who are not eligible for autologous stem cell transplant (ASCT).	C85	00774a	Tafasitamab: ODMS 01/04/2025 Lenalidomide: CDS

*This is for post 2012 indications only

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patient's individual clinical circumstances.

Tafasitamab is administered in combination with lenalidomide for a maximum of 12 cycles and is then continued as monotherapy until disease progression or unacceptable toxicity.

- Tafasitamab is administered by IV infusion at a dose of 12mg/kg on Days 1, 4, 8, 15 and 22 of Cycle 1; on Days 1, 8, 15 and 22 of Cycles 2 and 3; and on Days 1 and 15 of Cycle 4 onwards until disease progression or unacceptable toxicity.
- Lenalidomide is administered orally at a dose of 25 mg daily on Days 1 to 21, for up to 12 cycles or until disease progression or unacceptable toxicity, whichever comes first.

Each cycle is 28 days.

Facilities to treat anaphylaxis MUST be present when the systemic anti-cancer therapy (SACT) is administered.

Admin. Order	Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	1	Tafasitamab	12mg/kg	IV infusion[1,2]	250mL NaCl 0.9% over 150 minutes[3]	Cycle 1 only
1	4, 8, 15, 22	Tafasitamab	12mg/kg	IV infusion[1,2]	250mL NaCl 0.9% over 90 minutes[3]	Cycle 1 only
1	1, 8, 15, 22	Tafasitamab	12mg/kg	IV infusion[1,2]	250mL NaCl 0.9% over 90 minutes[3]	Cycles 2 and 3
1	1, 15	Tafasitamab	12mg/kg	IV infusion[1,2]	250mL NaCl 0.9% over 90 minutes[3]	Cycle 4 onwards
2	1-21 (no treatment days 22-28)	Lenalidomide	25mg	PO[4]	n/a	Cycle 1-12

[1] Tafasitamab must not be administered as an intravenous push or bolus. Tafasitamab must not be co-administered with other medicinal products through the same infusion line.

[2] The final concentration of the diluted solution should be between 2mg/ml to 8mg/ml of tafasitamab.

[3] For the first infusion of Cycle 1, the intravenous infusion rate should be 70 mL/hour for the first 30 minutes. Afterwards, the rate should be increased to complete the first infusion within a 150 minute period. Subsequent infusions are administered within a 90-120 minute period.

[4] Lenalidomide capsules should be taken at about the same time each day, in the evening may be preferred due to risk of drowsiness. The capsules should not be opened, broken or chewed. The capsules should be swallowed whole, preferably with water, either with or without food.
If less than 12 hours have elapsed since missing a dose of lenalidomide, the patient can take the dose.
If more than 12 hours have elapsed since missing a dose at the normal time, the patient should not take the dose, but take the next dose at the normal time on the following day.

Note: Administration volumes and fluids have been standardised to facilitate electronic prescribing system builds.

ELIGIBILITY:

- Indication as above
- ECOG 0-2
- Adequate renal, hepatic and haematological function

CAUTIONS:

- Tafasitamab is an anti-CD19 therapy; this should be considered if evaluating for CAR-T treatment or other CD19 targeted therapies.

EXCLUSIONS:

- Hypersensitivity to tafasitamab, lenalidomide or any of the excipients
- Pregnancy/breastfeeding
- Patients who are unable to comply with the Lenalidomide Pregnancy Prevention Programme

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist or by a Consultant Haematologist working in the area of haematological malignancies.

TESTS:

Baseline tests:

- FBC, renal and liver profile
- LDH, calcium, magnesium and phosphate
- Blood glucose (patients on oral hypoglycaemics)
- Blood pressure
- VTE risk assessment
- ECG
- Urine pregnancy testing or serum hCG test for women of childbearing potential as per Pregnancy Prevention Programme
- Assessment and registration as per Pregnancy Prevention Program for both male and female patients
- Thyroid function tests
- Virology screen* - Serology for Hepatitis B virus (HBV), [HBV sAg, HBV sAb, HBV cAb], Hepatitis C virus (HCV), human immunodeficiency virus (HIV), cytomegalovirus (CMV) [IgG] and Epstein–Barr virus (EBV)
  *See Regimen Specific Complications re Hepatitis B Reactivation

Regular tests:

- FBC monthly
- Renal and liver profile
- LDH, calcium, magnesium and phosphate
- Blood glucose (patients on oral hypoglycaemics)
- Blood pressure
- Urine pregnancy testing or serum hCG test every 28 days for women of childbearing potential as per lenalidomide Pregnancy Prevention Programme
- Consider monitoring thyroid function tests

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a consultant.
- Treatment with tafasitamab can be interrupted for the management of adverse reactions.
- Lenalidomide can be dose reduced as per Table 1 for the management of adverse reactions. Once reduced, the dose should not be re-escalated.
- Please refer to Table 2 for dose modifications for haematological toxicities, Table 3 for dose modifications for renal and hepatic impairment and Table 4 for dose modifications for adverse effects.

Table 1: Dose reduction steps for Lenalidomide modification

	Lenalidomide
Starting dose	25mg
Dose level -1	20mg
Dose level -2	15mg
Dose level -3	10mg
Dose level -4	5mg
Dose level -5	Discontinue*

*If lenalidomide is discontinued, treatment with tafasitamab monotherapy can continue

Haematological:

Table 2: Dose modification of tafasitamab and lenalidomide for haematological toxicities

Parameter	Dose modification
ANC (x10^9/L) <1.0 for at least 7 days	Withhold tafasitamab and lenalidomide and monitor complete blood count weekly until ANC ≥ 1.0 x10^9/L. Resume tafasitamab at the same dose and lenalidomide at a reduced dose if ANC returns to ≥ 1.0 x10^9/L. Refer to Table 1 for lenalidomide dose reduction steps.
ANC (x10^9/L) <1.0 with an increase of body temperature to ≥38°C	
ANC (x10^9/L) <0.5	
Platelets (x10^9/L) <50	Withhold tafasitamab and lenalidomide and monitor complete blood count weekly until platelet count is ≥ 50 x10^9/L. Resume tafasitamab at the same dose and lenalidomide at a reduced dose if platelets return to ≥ 50 x10^9/L. Refer to Table 1 for lenalidomide dose reduction steps.

Renal and Hepatic Impairment:

Table 3: Dose modification of tafasitamab and lenalidomide in renal and hepatic impairment

Drug	Renal impairment		Hepatic impairment	
Tafasitamab[a]	**CrCl (mL/min)**	**Dose modification**	**Impairment**	**Dose modification**
	≥30	No dose adjustment is needed	Mild	No dose adjustment is needed
	<30	No need for dose adjustment is expected	Moderate and severe	No need for dose adjustment is expected
	Haemodialysis	No need for dose adjustment is expected		
Lenalidomide[b]	**CrCl (mL/min)**	**Dose modification**	No need for dose adjustment is expected	
	30 to 50	Reduce dose to 10mg once daily*		
	<30 not requiring dialysis	15mg every other day		
	<30 requiring dialysis	Reduce dose to 5mg once daily. On dialysis days dose should be administered after dialysis.		

*The dose may be escalated to 15mg once daily after 2 cycles if patient is not responding to treatment and is tolerating the treatment	
[a]Renal and hepatic dose modifications from Giraud et al 2023. [b]Renal dose modifications from SmPC, hepatic dose modifications from Giraud et al 2023.	

Management of adverse events:

Table 4: Dose modification of tafasitamab for adverse effects

Adverse reaction	Severity	Dose modification
Infusion-related reactions	Grade 2 (moderate)	• Interrupt tafasitamab infusion immediately and manage signs and symptoms. • Once signs and symptoms resolve or reduce to Grade 1, resume tafasitamab infusion at no more than 50% of the rate at which the reaction occurred. If the patient does not experience further reaction within 1 hour and vital signs are stable, the infusion rate may be increased every 30 minutes as tolerated to the rate at which the reaction occurred.
	Grade 3 (severe)	• Interrupt tafasitamab infusion immediately and manage signs and symptoms. • Once signs and symptoms resolve or reduce to Grade 1, resume tafasitamab infusion at no more than 25% of the rate at which the reaction occurred. If the patient does not experience further reaction within 1 hour and vital signs are stable, the infusion rate may be increased every 30 minutes as tolerated to a maximum of 50% of the rate at which the reaction occurred. • If after rechallenge the reaction returns, stop the infusion immediately.
	Grade 4 (life-threatening)	• Stop the infusion immediately and permanently discontinue tafasitamab.

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

- As outlined in NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting - Available on the NCCP website

Tafasitamab: Low **(Refer to local policy)**
Lenalidomide: Minimal to low **(Refer to local policy)**

For information:
Within NCIS regimens, antiemetics have been standardised by Medical Oncologists and Haemato-oncologists and information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) - Available on the NCCP website
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - Available on the NCCP website

PREMEDICATIONS:

Lenalidomide: Not usually required

Tafasitamab:

- A pre-medication to reduce the risk of infusion-related reactions (IRR) should be administered 30 minutes to 2 hours prior to tafasitamab infusion. Refer to Table 5 for suggested premedications. To note a pre-medication time of 60 minutes before the tafasitamab dose has been chosen in Table 5 to facilitate the NCIS build.
- If a patient has experienced a Grade 1 to 3 IRR, pre-medication should be administered before subsequent tafasitamab infusions.
- For patients not experiencing IRR during the first three infusions, pre-medication is optional for subsequent infusions.

Table 5: Suggested premedications prior to tafasitamab infusion

Drugs	Dose	Route
Paracetamol	1g	PO 60 minutes prior to tafasitamab infusion
Chlorphenamine	4mg	PO 60 minutes prior to tafasitamab infusion
Dexamethasone	16mg	PO 60 minutes prior to tafasitamab infusion
Famotidine	20mg	PO 60 minutes prior to tafasitamab infusion

OTHER SUPPORTIVE CARE:

- In case of neutropenia, the consultant may consider the use of growth factors in patient management.
- **Thromboprophylaxis:** Prophylactic antithrombotic medicines should be recommended, especially in patients with additional thrombotic risk factors. Patients should be instructed to seek medical care if they develop symptoms such as shortness of breath, chest pain, arm or leg swelling. Prophylactic antithrombotic medicine options include single agent aspirin, or prophylactic doses of low molecular weight heparin (LMWH) or direct oral anti-coagulant (DOAC) **(Refer to local policy).**
- Both diarrhoea and constipation are common side effects associated with treatment. Patients may require either laxatives or anti-diarrhoeals. Consider use of cholestyramine 4g OD in patients with lenalidomide-associated diarrhoea **(Refer to local policy).**
- Tumour Lysis Syndrome prophylaxis **(Refer to local policy).**
- Male patients must use condoms during treatment, during dose interruption and for at least 7 days following discontinuation of treatment if their partner is pregnant or is of childbearing potential not using effective contraception. Male patients should not donate semen or sperm during treatment (including during dose interruptions) and for at least 7 days following discontinuation of lenalidomide.

ADVERSE EFFECTS:

- Please refer to the relevant Summary of Product Characteristics for details.
- **Tafasitamab and lenalidomide are subject to additional monitoring. Healthcare professionals are asked to report any suspected adverse reactions.**

REGIMEN SPECIFIC COMPLICATIONS:

- **Hepatitis B Reactivation:** Patients should be tested for both HBsAg and HBcoreAb as per local policy. If either test is positive, such patients should be treated with anti-viral therapy (Refer to local infectious disease policy). These patients should be considered for assessment by hepatology.
- **Venous and arterial thromboembolic events:** Patients with known risk factors for thromboembolism, including prior thrombosis, should be closely monitored.
- **Progressive Multifocal Leukoencephalopathy (PML):** Progressive multifocal leukoencephalopathy (PML) has been reported during combination therapy with tafasitamab. Patients should be monitored for new or worsening neurological symptoms or signs that may be suggestive of PML. If PML is suspected, further dosing of tafasitamab must be immediately suspended. If PML is confirmed, tafasitamab must be permanently discontinued.
- **Teratogenetic effects**: Lenalidomide is structurally related to thalidomide, a powerful human teratogen. Lenalidomide must never be used by women who are pregnant or by women who could become pregnant unless all the conditions of the Lenalidomide Pregnancy Prevention Programme are met. These conditions must be fulfilled for all male and female patients.
- **Skin reactions**: Lenalidomide must be discontinued permanently for exfoliative or bullous rash or if Stevens-Johnson syndrome (SJS), Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) or toxic epidermal necrolysis (TEN) is suspected.

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information.

COMPANY SUPPORT RESOURCES/Useful Links:

Please note that this is for information only and does not constitute endorsement by the NCCP

Lenalidomide

- Please refer to the HPRA website (www.hpra.ie) for the individual product for list of relevant support resources
- Prescribers are required to read and understand the relevant HCP Information Guide and to adhere to the PPP

REFERENCES:

1. Salles G et al. Tafasitamab plus lenalidomide in relapsed or refractory diffuse large B-cell lymphoma (L-MIND): a multicentre, prospective, single-arm, phase 2 study. Lancet Oncol. 2020 Jul;21(7):978-988. doi: 10.1016/S1470-2045(20)30225-4. Epub 2020 Jun 5. PMID: 32511983.
2. Duell J et al. Long-term outcomes from the Phase II L-MIND study of tafasitamab (MOR208) plus lenalidomide in patients with relapsed or refractory diffuse large B-cell lymphoma. Haematologica. 2021 Sep 1; 106(9):2417-2426. doi: 10.3324/haematol.2020.275958. PMID: 34196165; PMCID: PMC8409029.
3. Zinzani PL et al. RE-MIND: Comparing Tafasitamab + Lenalidomide (L-MIND) with a Real-world Lenalidomide Monotherapy Cohort in Relapsed or Refractory Diffuse Large B-cell Lymphoma. Clin Cancer Res. 2021 Nov 15; 27(22):6124-6134. doi: 10.1158/1078-0432.CCR-21-1471. Epub 2021 Aug 25. PMID: 34433649.
4. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V5 2023. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf
5. Tafasitamab (Minjuvi®). Summary of Product Characteristics. Last updated: 17/09/2024. Accessed 17/02/2025. Available at: https://www.ema.europa.eu/en/documents/product-information/minjuvi-epar-product-information_en.pdf
6. Lenalidomide (Revlimid®). Summary of Product Characteristics. Last updated: 08/01/2024. Accessed 17/02/2025. Available at: https://www.ema.europa.eu/en/documents/product-information/revlimid-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	01/04/2025		Dr Amjad Hayat

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